Who Needs an STD Test? National Guidelines for STD Screening

Gail Bolan MD
Chief, STD Control Branch
CA Department of Public Health
October 25, 2007

Overview of Presentation

- Screening Definitions
  - Risk Screening
  - Testing to identify asymptomatic infection
- Principles of Screening
  - Uses and Abuses
- National Screening Recommendations
  - Disease Specific
    - Chlamydia, GC, Syphilis, HSV, HPV
  - Population Specific
    - Young women, pregnant women, young men, MSM

Providers' Questions About Screening for STDs

- Who, What, Where, and When
- Do I need to treat if *asymptomatic*?
- Do I need to treat patient's sex partners?
- How much time?
- Who pays?

Patients' Questions about STD Testing

"I'd just like to be tested

……for everything."

Risk Screening Issues

- Sexual history taking and risk reduction client centered counseling including the 5 P's
  - Partners
  - Practices
  - Past History of STDs
  - Protection for STDs
  - Pregnancy prevention
- Patients should be informed about which STDs they are tested for (and which not) and if positive which must be reported to the local HD

Sexual History Taking: The 5 P's

1. Partners
   - Do you have sex with men, women or both?
   - In the past 12 months how many partners have you had sex with?
   - In the past 2 months how many partners have you had sex with?
2. Pregnancy prevention
   - Are you or your partner trying to get pregnant?
   - If no, What are you doing to prevent pregnancy?
3. Protection from STDs
   - What do you do to protect yourself from STDs and HIV?

Sexual History Taking: The 5 P's

4. Practices

To understand your risks for STDs, I need to understand the kind of sex you have had recently.

- Have you had vaginal sex, meaning penis in the vagina sex? If yes, do you use condoms never, sometimes or always?
- Have you had anal sex, meaning penis in the rectum/anus/butt sex? If yes, do you use condoms never, sometimes or always?
- Have you had oral sex, meaning mouth on penis/vagina/rectum sex? If yes, do you use condoms never, sometimes or always?
- For condoms: if never: Why don't you use condoms? If sometimes: In what situations or with whom do you use or not use condoms?

5. Past History of STDs

- Have you ever Had an STD?
- Have any of your partners had an STD?

- Additional questions to identify HIV and Hepatitis risk
  - Have you or any of your partners ever injected drugs
  - Have you or any of your partners exchanged money or drugs for sex

- Is there anything else about your sexual practices that I need to know about?

Diagnostic Tests vs. Screening

Diagnostic Tests

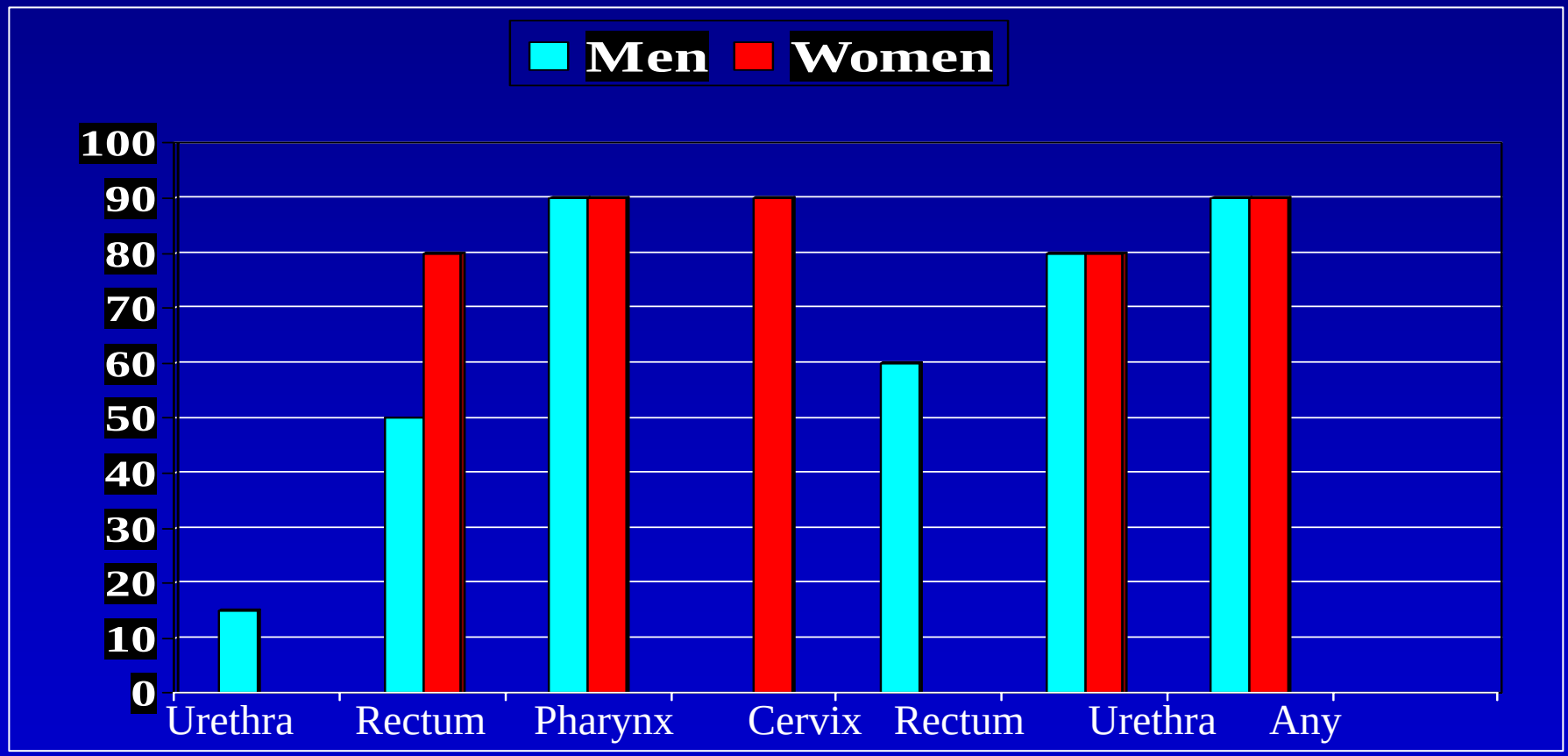
- **Goal:** identify reason for signs, symptoms, and patient complaints

Screening

- **Goal:** identify asymptomatic disease in apparently healthy people

Why Bother Screening for STD?

Percent of Persons with STD Who Are Asymptomatic



Factors to Consider when Designing a Cost-effective Screening Program

- Prevalence of disease in population
- Sensitivity and specificity of screening criteria
- Test performance characteristics of diagnostic test
- Cost of test
- Cost of treatment and complications

STD Testing Modalities

- Culture
  - Chlamydia, gonorrhea, herpes
- Antigen-based tests
  - Chlamydia, gonorrhea
- Non-amplified DNA probe
  - Chlamydia, gonorrhea (GenProbe Pace-2 ®)
- Nucleic Acid Amplification tests (NAATS)
  - Chlamydia, gonorrhea
  - Cervix, urethra, urine
    - Roche *Amplicor* (PCR)
    - GenProbe *Aptima (*TMA)
    - B-D *ProbeTec* (SDA)
  - Self-collected vaginal swabs (Aptima)
  - Liquid-based cytology sample (Thin-Prep ® or SurePath® for Aptima ® and Amplicor ® GC/CT as well as HPV)
- Serologic tests (syphilis, herpes, Hepatitis B)

Uses and Abuses of Screening Tests

- Screening tests are ubiquitous in practice
- Principles of screening are widely misunderstood
- ***Goal of screening is to test apparently well people to find those at increased risk of a disease or disorder***
- Inappropriate screening is harmful
  - Injurious to one's health
  - Stigmatizing
  - Costly

(Grimes, Lancet 2002)

When Earlier Diagnosis is Worth the Cost ?

- If improves survival or quality of life
- If the clinician has the time to manage the Dx before Sx develop
- If the patient with an earlier Dx will comply with intervention
- If the screening program effectiveness has been established
- If the test cost, accuracy and acceptability are acceptable to the patient and society

(Sackett, Clinical Epidemiology: a basic science for clinical medicine)

National Screening Recommendations

- US Preventive Services Task Force
- Centers For Disease Control
- ACOG
- AMA
- Other medical organizations

Clinic-based Chlamydia Screening Recommendations- Non Pregnant Women

US Preventive Services Task Force, 2007

- Sexually active women age 24* and younger should be screened annually
- Women age 25* and older should be screened "if increased risk"
  - Risk factors: Previous CT or other STDs, new or multiple partners, inconsistent condom use, sex work
  - Demographics: African Americans and Hispanics

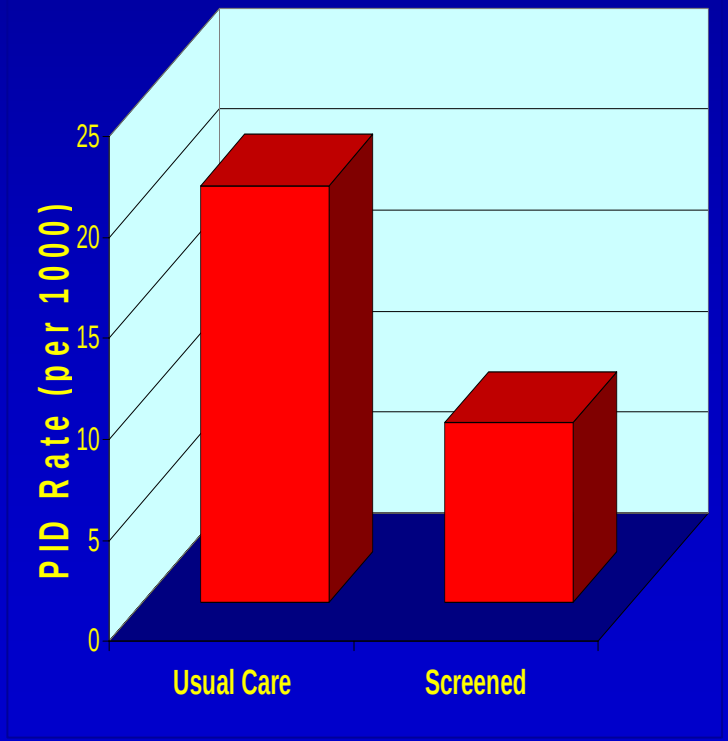
Endorsed by the CDC, ACOG & other medical associations

As of 2000, NCQA HEDIS measure

* In 2001, the age cut off was 25 years

CT Screening Prevents PID:
Clinical trial, Seattle HMO, 1990-1992

- Randomized controlled trial
- 1009 high risk women 18-34 assigned to intervention (invitation to get tested) & 1598 to usual care



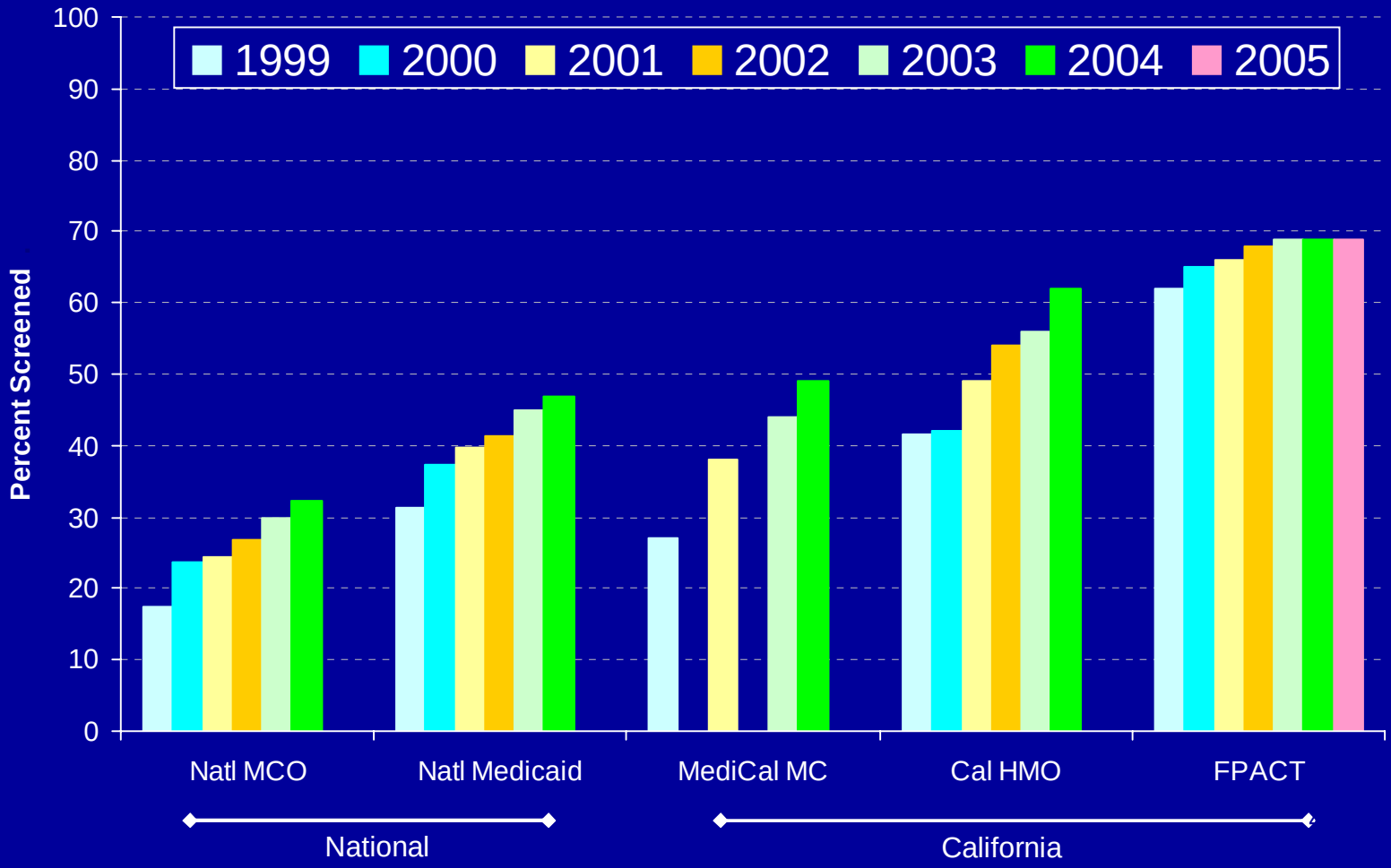
- Among intervention group, 64% were tested and 7% were positive and treated
- Outcome of PID w/i 1-year: 9 cases in screening group, 33 cases in usual care group (RR=0.44 (0.20-0.90))

Scholes et al., NEJM, 1996; 334:1362-6

Recommend Nucleic Acid Amplification Tests for Detecting Chlamydia and Gonorrhea

- Highest sensitivity
  - Able to detect up to 40% more CT infections
  - Less dependent on specimen collection and handling
- Noninvasive
  - Urine and self-collected vaginal swabs
- Non-clinical settings
  - Pelvic and genital exams not necessary
    - Clinic intake areas
    - Community based organizations
    - Home testing

Estimated Chlamydia Screening Coverage (HEDIS), Females 16–26 U.S.A. and California, 1999–2005



Source: National Committee on Quality Assurance; California DHS Division of Medi-Cal Managed Care; Kaiser Permanente Northern CA; California DHS Office of Family Planning

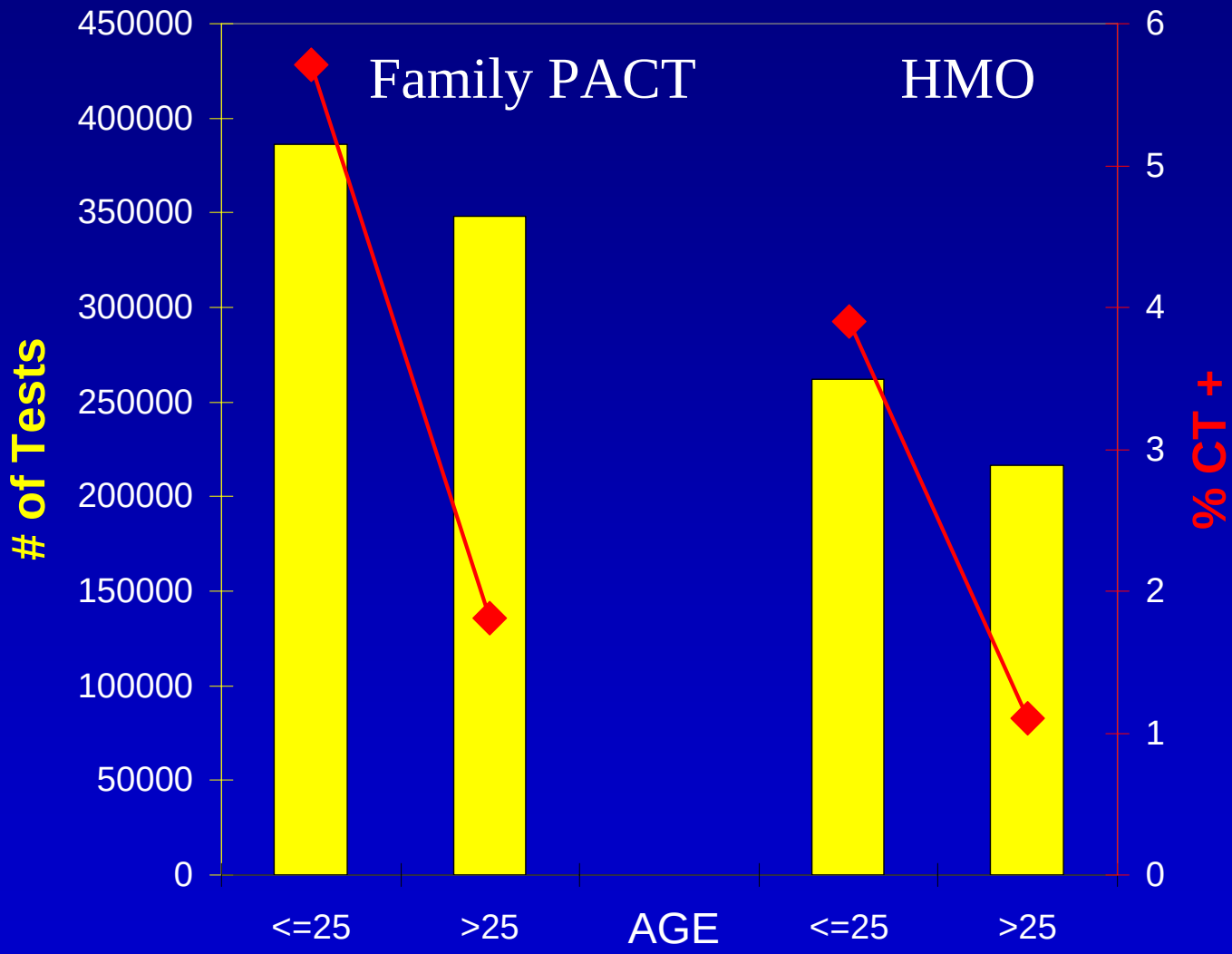
Are we screening the wrong women?

- The some women in the target age range (24 and younger) are NOT being screened

Meanwhile

- A large proportion of current testing is being done for women over age 24
- Guidelines for screening women over 25 are not specific
  - Other women “at risk” such as prior history of CT or other STDs, new or multiple partners, or inconsistent condom use

Chlamydia Test Volume and Prevalence by Age among Female Patients in Public and Private Clinics



Source: **PUBLIC: Family PACT, January-June 2001 & Infertility Prevention Project 2003**
PRIVATE: PHIP - Kaiser Permanente, managed care organization, 1999-2002

Proposed CT Diagnostic Guidelines for Women > Age 25 in California

- Diagnostic testing based on clinical indications:
  - Current contact (exposure) to any STD
  - Clinical signs of cervicitis or PID
  - Newly confirmed or presumptively treated other STD dx
- Targeted Screening based on risk factors:
  - Partner possible other partners during past 12 mos!!!
  - More than 1 partner during past 12 mos
  - New partner during past 2-3 mos
- Additional discussion: higher CT risk often associated with younger age – emphasis on prioritizing age 26-30

Clinic-based Chlamydia Screening Recommendations- Pregnant Women

US Preventive Services Task Force, 2007

- Pregnant women age 24 and younger should be at the first prenatal visit
- Pregnant women age 25 and older should be screened “if increased risk”
  - Risk Factors: Previous CT or other STDs, new or multiple partners, inconsistent condom use, sex work
  - Demographics: African Americans and Hispanics
- If continued risk factors or new risk then screen in the 3rd trimester

CDC Treatment Guidelines, 2006

- All pregnant women at the first prenatal visit
- Pregnant women age 24 and younger and those “at increased risk” should be retested during the third trimester
  - New or more than one sex partner

Chlamydia Screening in Heterosexual Males

- Screening in heterosexual males not routinely recommended
- Need evidence of reduction of infection in women to be cost effective
- However, selective screening in high prevalence clinics (e.g. adolescent, corrections, STD) may be beneficial
- Modeling suggests prevalence among males should be at least 6%*
- CDC will develop separate guidance in this area*

** Discussed at the 2006 Guidelines Meeting*

Chlamydia Treatment
Adolescents and Adults

Recommended regimens:

- Azithromycin 1 g PO x 1
- Doxycycline 100 mg PO BID x 7 d

Alternative regimens:

- Erythromycin base 500 mg PO QID x 7 d
- Erythro ethylsuccinate 800 mg PO QID x 7 d
- Ofloxacin 300 mg PO BID x 7 d
- Levofloxacin 500 mg PO QD x 7 d

**** NO CHANGES FOR 2006 GUIDELINES ****

Clinic-based Gonorrhea Screening Recommendations

US Preventive Services Task Force, 2005

- Sexually active women including pregnant women at the first prenatal visit should be screened “if increased risk”
  - Age 24 or younger
  - Risk Factors: Previous GC or other STDs, new or multiple partners, inconsistent condom use, sex work, drug use
  - Demographics: African Americans
- Pregnant women with continued risk or new risk should be screened in the 3rd trimester

CDC Treatment Guidelines, 2006

- Follows the US Preventive Services Task Force Recommendations
- All pregnant women at risk for gonorrhea or living in an area in which the prevalence of GC is high should be screened at the first prenatal visit and in the third trimester if continued risk

California Gonorrhea Screening and Diagnostic Testing Guidelines for Non-Pregnant Female Patients

Annual Screening *

- All sexually active females 25 years and younger

Targeted Screening based on risk factors if over 25 yrs of age

- Hx of GC in 2 yrs, multiple partners in 12 mos, partner with other partner, African American women 26-30

Diagnostic Testing

- When clinical exam findings indicate gonococcal infection: cervicitis, pelvic inflammatory disease, or disseminated gonococcal infection.

Contact Testing

- For patients who report contact/exposure to any sexually transmitted disease (STD)

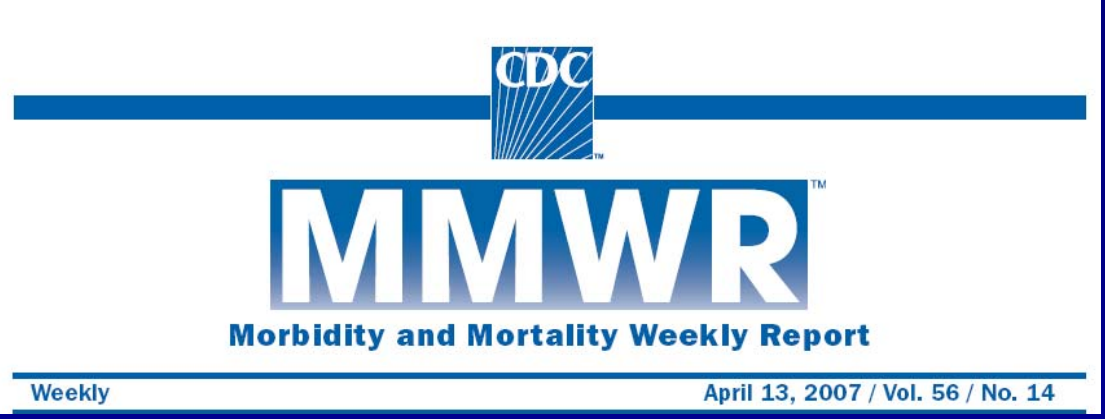
Testing for Co-Infections

- For patients with a newly diagnosed STD

Repeat Screening

- Three to six months after treatment, patients should have a repeat test for re-infection.

** Only if the prevalence is at least 1%.*



Gonorrhea Treatment, 2007

Recommended regimens:

- Ceftriaxone 125 mg IM x 1
- Cefixime 400 mg PO x 1
  - Currently available only as suspension
- ~~Ciprofloxicin 500 mg PO x 1~~
- ~~Ofloxacin 400 mg PO x 1~~
- ~~Levofloxacin 250 mg PO x 1~~

Alternative regimens:

- **Cefpodoxime 400 mg po x 1**
- **Cefuroxime 1 g po x 1**
- Spectinomycin 2 g IM x 1: not available
- Single-dose injectable cephalosporin regimens
- Azithromycin 2 gm PO

Co-treat for chlamydia unless ruled out *with highly sensitive test (NAAT)*

MMWR April 13, 2007; 56 (14)

Recommendations for Chlamydia and Gonorrhea Re-Testing after Treatment

- Prefer “re-testing” to “re-screening”
- High rates of re-infection after treatment and for GC may confer an elevated risk of PID
- Consider re-testing of females; some experts suggest re-testing of males for CT and consider re-testing of males for GC
- Time frame: 3 months after treatment and for GC whenever seek care within 12 months if did not return at 3 months
- No test of cure except in pregnant women with CT and for GC if treated initially with a fluoroquinolone and symptoms persist or recur after treatment

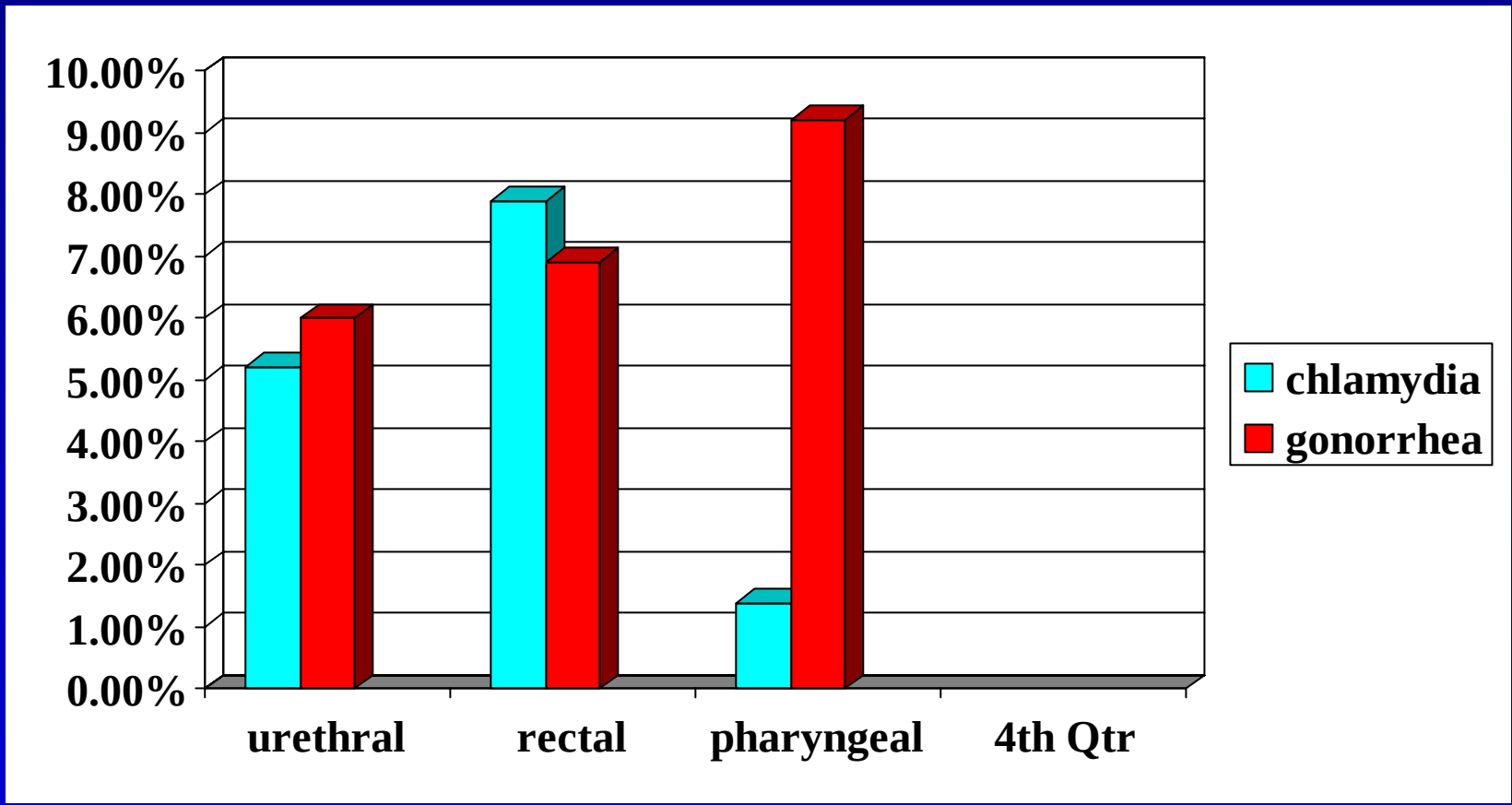
STD Screening for MSM

STD	Site	Type of Sex
HIV	blood	oral, anal
Syphilis	blood	oral, anal
GC/CT	urethra or urine	oral, anal
GC/CT	rectum	receptive anal
GC	pharynx	receptive oral
HSV-2*	blood	

* Some experts recommend

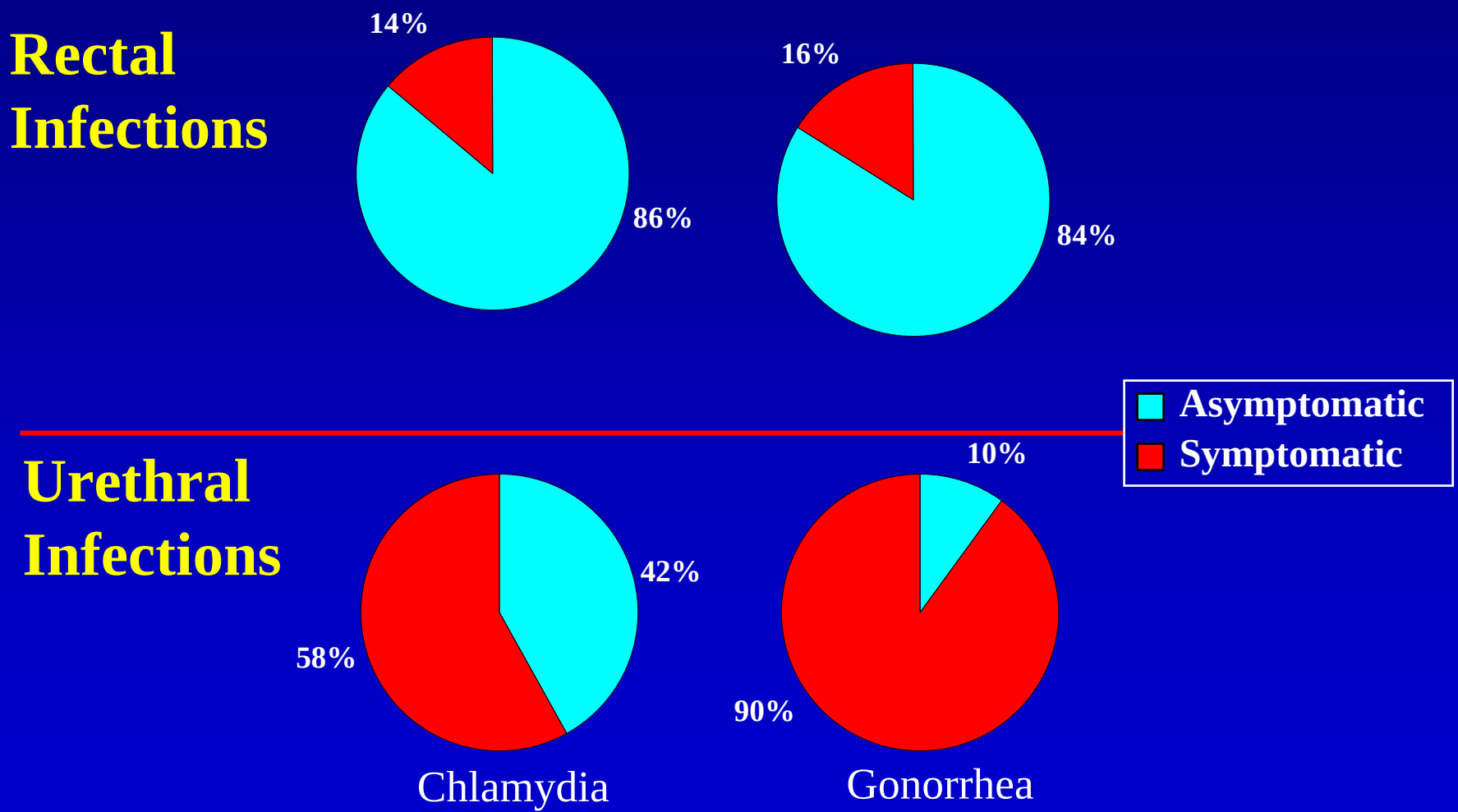
FREQUENCY: At least at the initial visit then annually or more frequently based on risk

How common are rectal and pharyngeal CT and GC infections in MSM?



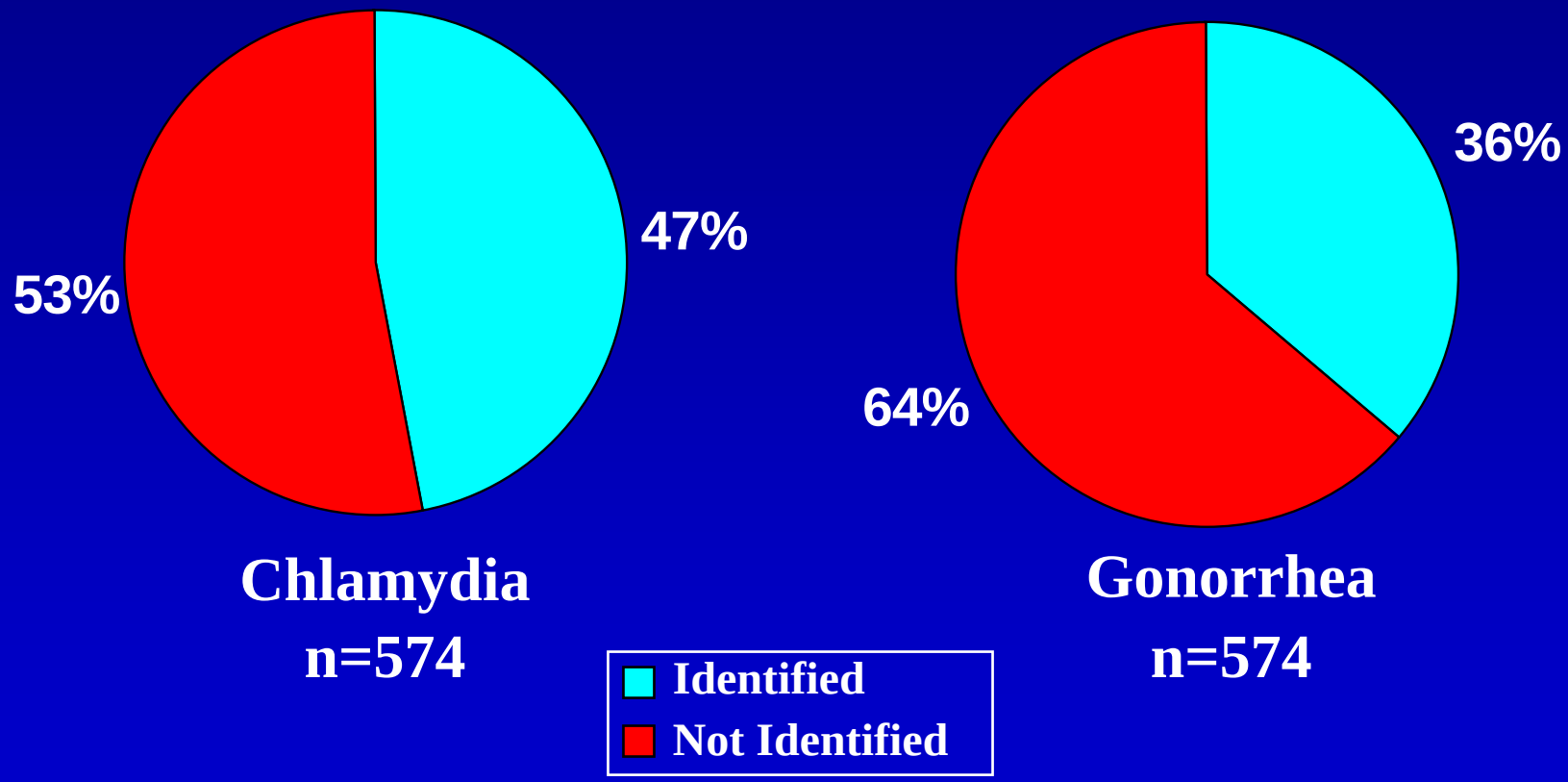
Kent, CK et al, *Clin Inf Dis*, July 2005

Proportion of asymptomatic rectal and urethral chlamydial and gonococcal infection among MSM– San Francisco, 2003



Kent, CK et al, *Clin Inf Dis*, July 2005

Proportion of chlamydial and gonococcal infections not identified if only urine/urethral screening performed among MSM – San Francisco, 2003



Kent, CK et al, *Clin Inf Dis,* July 2005

C. trachomatis NAAT Testing

…*not* FDA-cleared for rectal or pharyngeal specimens

Syphilis Screening Recommendations

US Preventive Services Task Force, 2004

- All pregnant women should be screened at the first prenatal visit and pregnant women at high risk should be screened in the 3rd trimester and at delivery
- Persons should be screened “if increased risk”
  - Demographics: MSM, African Americans, incarcerated persons, communities with high syphilis morbidity
  - Risk Factors: sex work, exchange sex for drugs, diagnosed with other STDs

CDC Treatment Guidelines, 2006

- All pregnant women should be screened at the first prenatal visit
- Pregnant women at high risk for syphilis, live in areas of high syphilis morbidity, are previously untested, or have positive serology in the first trimester should be screened again early in the third trimester and at delivery.

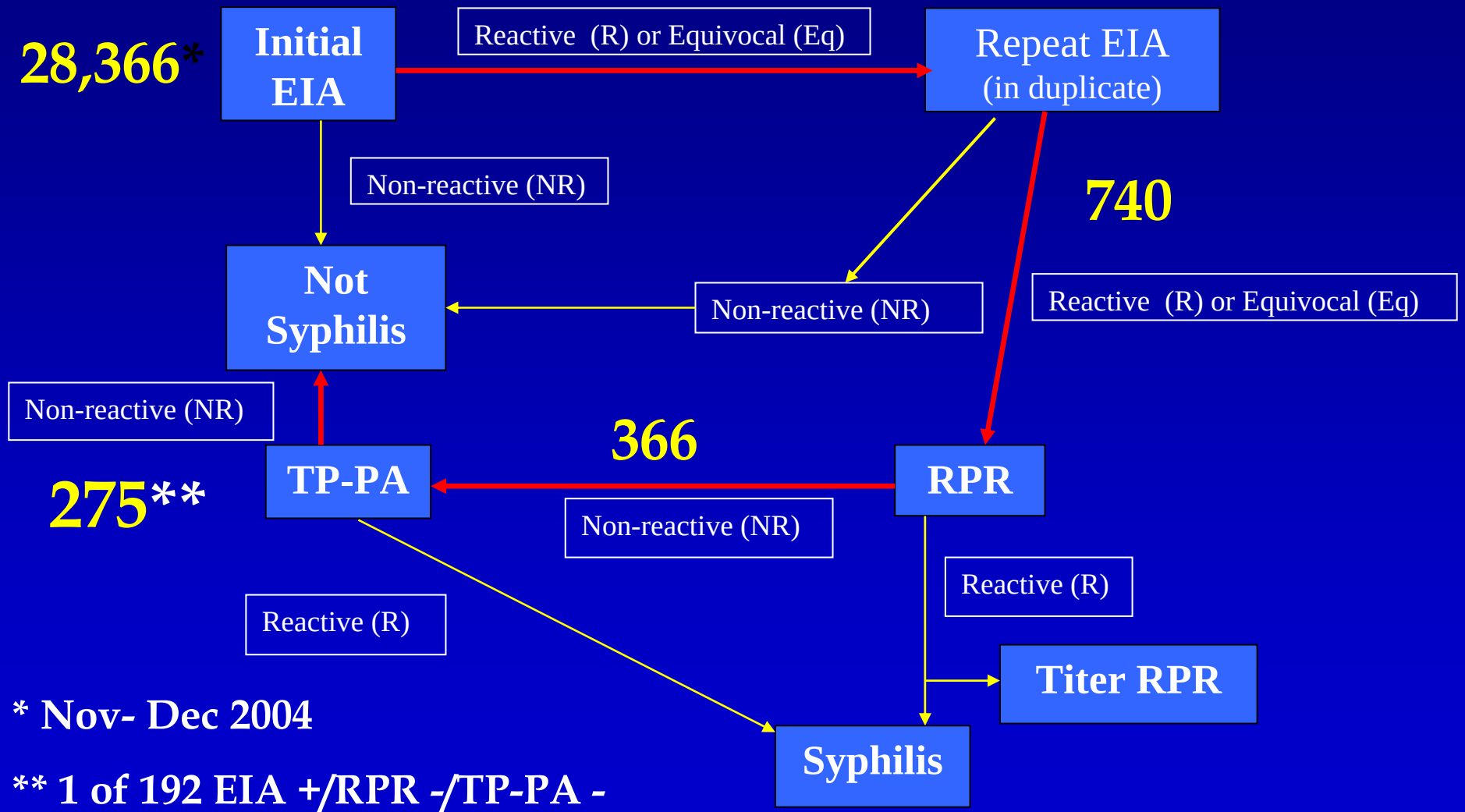
Screening Tests for Syphilis

- Non treponemal tests
  - VDRL/RPR
- Treponemal tests
  - FTA-abs / TP-PA (MHA-TP)
  - EIA
    - Captia, Trep-Chek, Trep-Sure, Liaison

Syphilis EIA Treponemal Tests

- Treponemal tests FDA cleared for clinical use
- Can be used for screening but if positive then need quantitative reflexive RPR/VDRL for clinical management
- Both IgM and IgG tests available
  - No clinical value of IgM in adult early syphilis diagnosis
- Advantages
  - No prozone, low cost, automated, and less lab occupational hazard (pipeting)
- Disadvantages
  - Studies to compare test performance with TP-PA are needed
    - Sensitivity and Specificity concerns regarding Captia
    - Specificity concerns regarding Trep-Chek

Syphilis EIA Trep- Chek Testing Algorithm: Southern Kaiser



* Nov- Dec 2004

** 1 of 192 EIA +/RPR -/TP-PA - confirmed by CDC Immunoassay

Novak et al, ASM 2006

Kaiser Syphilis EIA Screening Algorithm, 2005

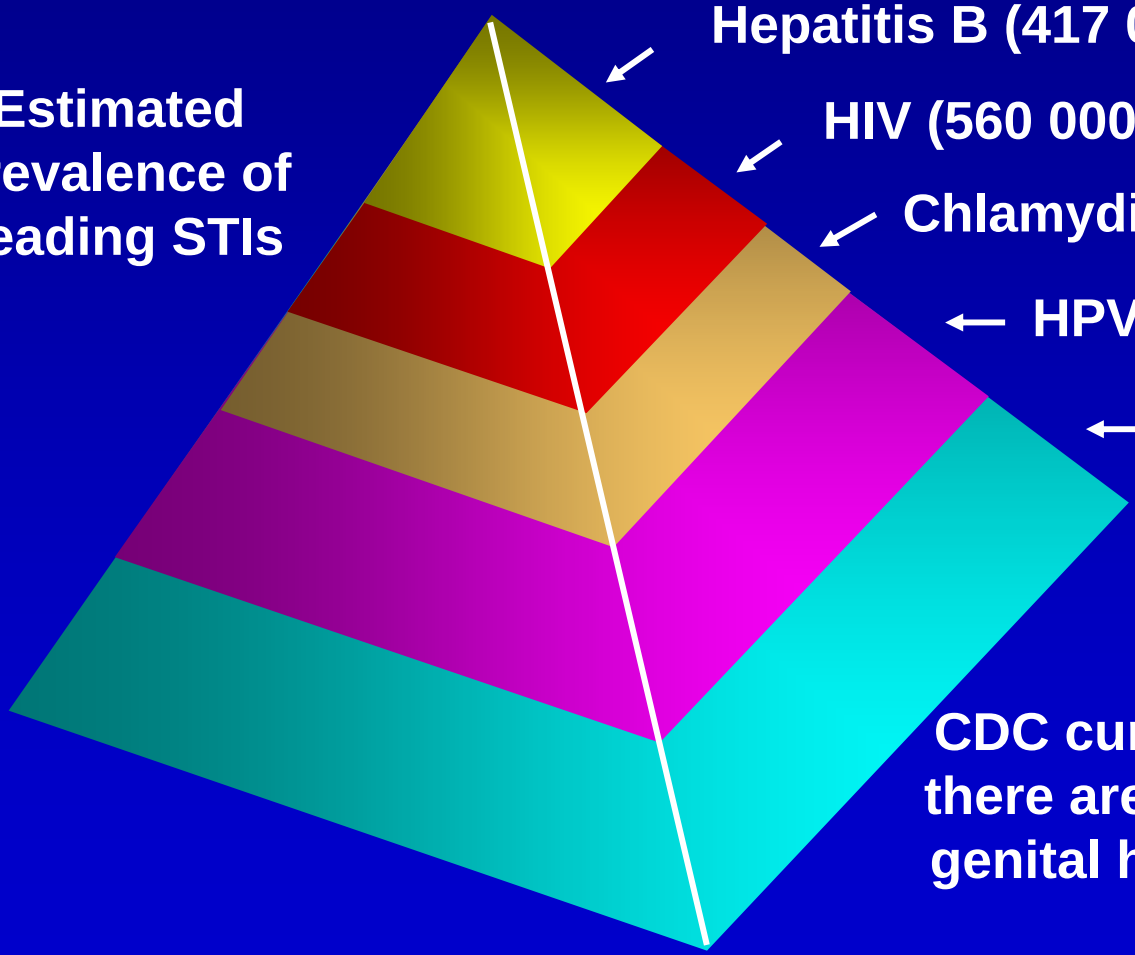
- Screen with EIA and repeat positives/equivocals
- If positive x 2, reflexive quantitative RPR/VDRL
- If negative RPR/VDRL, reflexive TP-PA
- Positive predictive value of a positive EIA for syphilis with a negative RPR and TP-PA is low
- Lab reports as unconfirmed positive EIA test which most likely represents a false positive results
- If patient is low risk for syphilis no further follow-up
- If patient is high risk for syphilis, advise to repeat serologic test in one 1 month

Syphilis Treatment

- Primary, secondary & early latent
  - Benzathine PCN G (L-A) single dose IM 2.4 million units
    - Do not use other PCN formulations!
    - Do not use azithromycin
  - Doxycycline 100 mg PO bid x 14 days (inferior)
  - Ceftriaxone 1 g IV or IM daily x 8-10 days (inferior)
- Late latent or unknown duration
  - Benzathine PCN G IM 2.4 million units weekly x 3 doses (7.2 million u total)
  - Doxycycline 100 mg PO bid x 28 days (inferior)

Herpes: the Most Prevalent STI in the USA

Estimated Prevalence of Leading STIs



Hepatitis B (417 000)

HIV (560 000)

Chlamydia (2 million)

HPV (20 million)

Herpes (50 million)

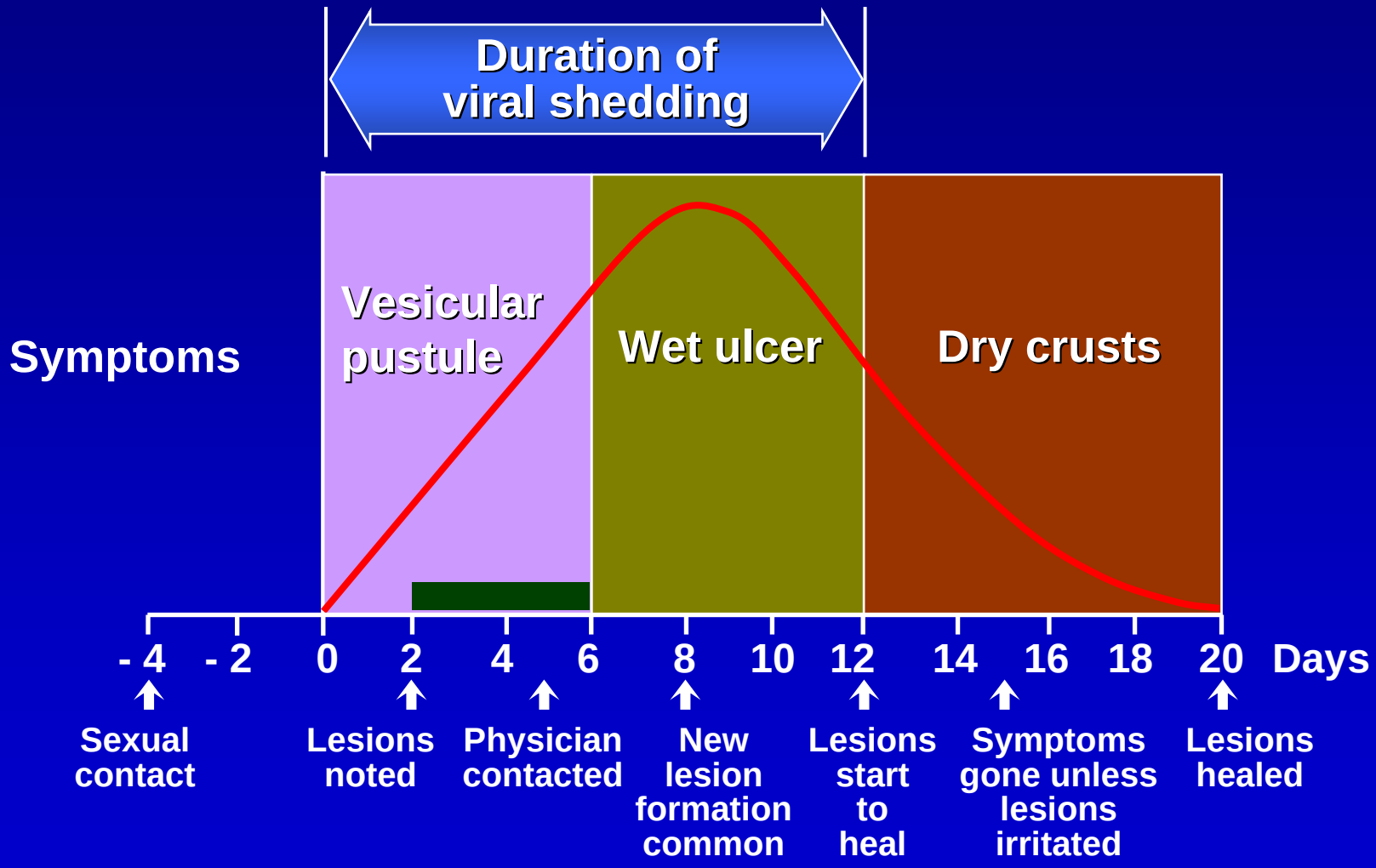
CDC currently estimates there are one million new genital herpes infections per year

Herpes Simplex Virus

- HSV-1
  - Mostly orolabial (cold sores, fever blisters)
  - An increasing proportion of cases of primary genital herpes (15-30%)
- HSV-2
  - Almost entirely genital; oral infection rare
  - >95% of recurrent genital herpes
  - Contributes to HIV transmission

Corey L, et al. STD. 1999:285-312.

Clinical Course of Primary Herpes Infection



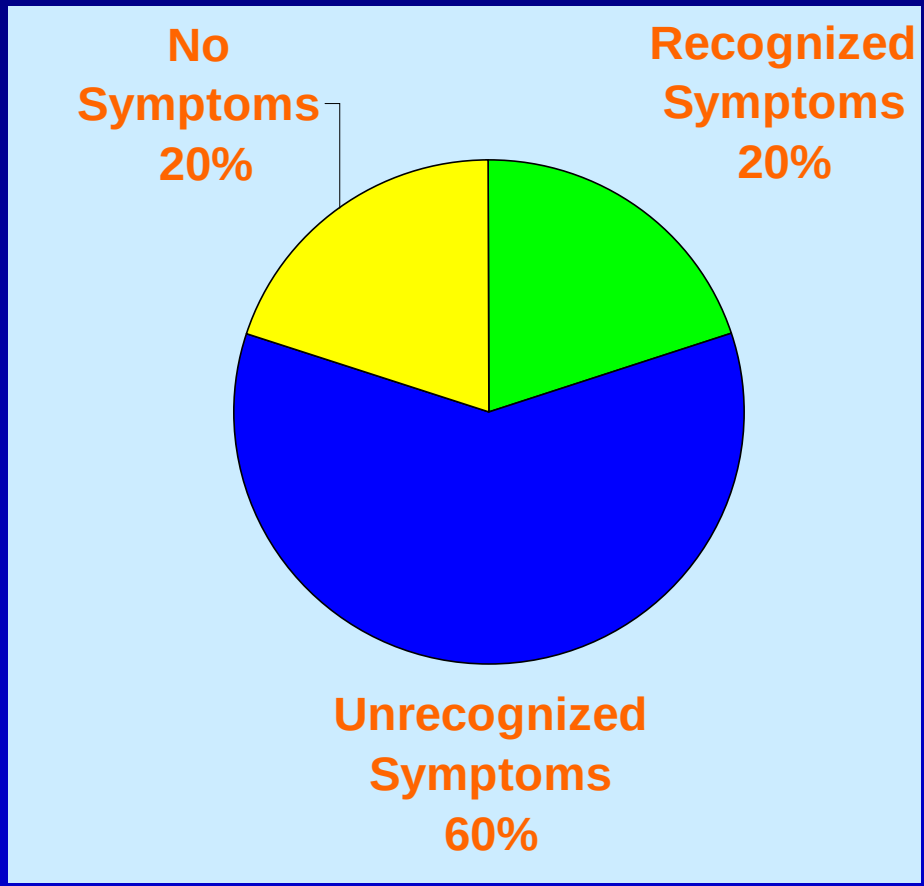
Corey L, et al. Sexually Transmitted Diseases. 1999:285-312.

Asymptomatic HSV Shedding

- Intermittent subclinical shedding occurs in 95% of people with genital HSV-2
  - Present 5-70% of days in persons with genital HSV-2
  - Frequency highest in first year after infection (20 - 30% of days), but how high it remains probably depends on how often you measure it--may be majority of days
  - Similar frequency in persons with and without recognized symptoms
- Uncommon in HSV-1 genital infection

Subclinical/Asymptomatic Herpes

- Only 20% of people seropositive for HSV-2 recognize their infection
- 60% have unrecognized or atypical infections
- 20% have no symptoms



What They Say They Think They Have

MEN

- Folliculitis
- Jock itch
- “Normal” itch
- Zipper burn
- Hemorrhoids
- Allergy to condoms
- Prostatitis
- Irritation from
  - Tight jeans
  - Sexual intercourse
  - Bike seat
- Insect or spider bites

WOMEN

- Yeast infection
- Vaginitis
- UTI
- Menstrual complaint
- Hemorrhoids
- Heat rash
- Post-coital soreness
- An ingrown hiar
- Allergy to
  - Condom
  - Sperm
  - Spermicide
  - Pantyhose
- Irritation from
  - Douching
  - Shaving
  - Bike seat

Arguments for HSV-2 Serologic Screening

- Up to 80% of those seropositive for HSV-2 unaware of their infection
- Of these, 75% atypical, 25% asymptomatic
- Patients can be taught to recognize symptoms; treat as needed
- Patients may be motivated to reduce risk behavior and/or protect partners and reduce transmission

Arguments Against HSV-2 Serologic Screening

- Unproven benefit
  - May not change clinical management
  - Effect on sexual risk behavior unknown
- Potential significant costs
  - Expensive ($20-60)
  - Potential for adverse psychological impact
  - Increase demand on health care system

Type-Specific* gG-based HSV Serology Tests

- HSV-1 and HSV-2 Immunoblot IgG (Focus Technologies- HerpeSelect)
  - Sensitivity 97-100%, Specificity 96-97%
- HSV-1 and HSV-2 ELISA IgG (Focus Technologies- HerpeSelect)
  - Sensitivity 96-100%, Specificity 94-98%
- Captia ELISA HSV-2 (Trinity Biotech)
  - Sensitivity 90-92%, Specificity 91-98%
- Biokit HSV-2 & SureVue HSV-2 (Biokit & Fisher Scientific) Point of care tests
  - Sensitivity 93-96%, Specificity 95-98%

GOLD STANDARD: Western Blot (>99% sensitivity and specificity)

** Note: Older non-specific tests are still on the market.*

HSV Screening and Testing Recommendations

US Preventive Services Task Force, 2005

- Routine serologic screening of asymptomatic persons is not recommended
- Routine serologic screening of asymptomatic pregnant women is not recommended

CDC Treatment Guidelines, 2006

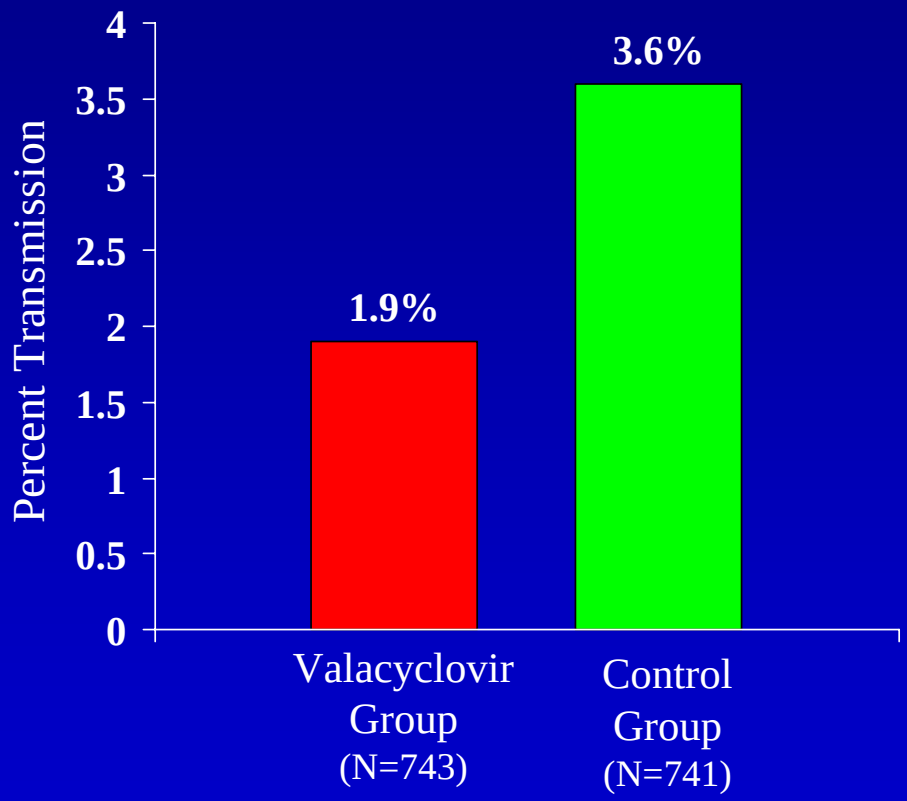
- HSV-2 serology tests may be useful in the following situations
  - Clinical diagnosis without lab confirmation
  - Patients with a partner with genital HSV
- Some experts recommend serologic tests:
  - As part of “comprehensive STD evaluation” in high risk individuals such a those with multiple partners, HIV-infected, MSM with high HIV risk
  - In pregnant women with no history of HSV and a partner with history of symptomatic HSV
- Universal screening is not recommended

HSV Transmission: Discordant Couples

- Research with discordant couples estimates sexual transmission to be ~11-12% per year
  - 14-17% male to female
  - 4-6% female to male
- Most (~70%) sexual transmission occurs during asymptomatic shedding
- Consistent and correct condom use decreases risk of transmission
- Suppression shown to reduce risk of transmission by ~50%; new FDA-approved indication

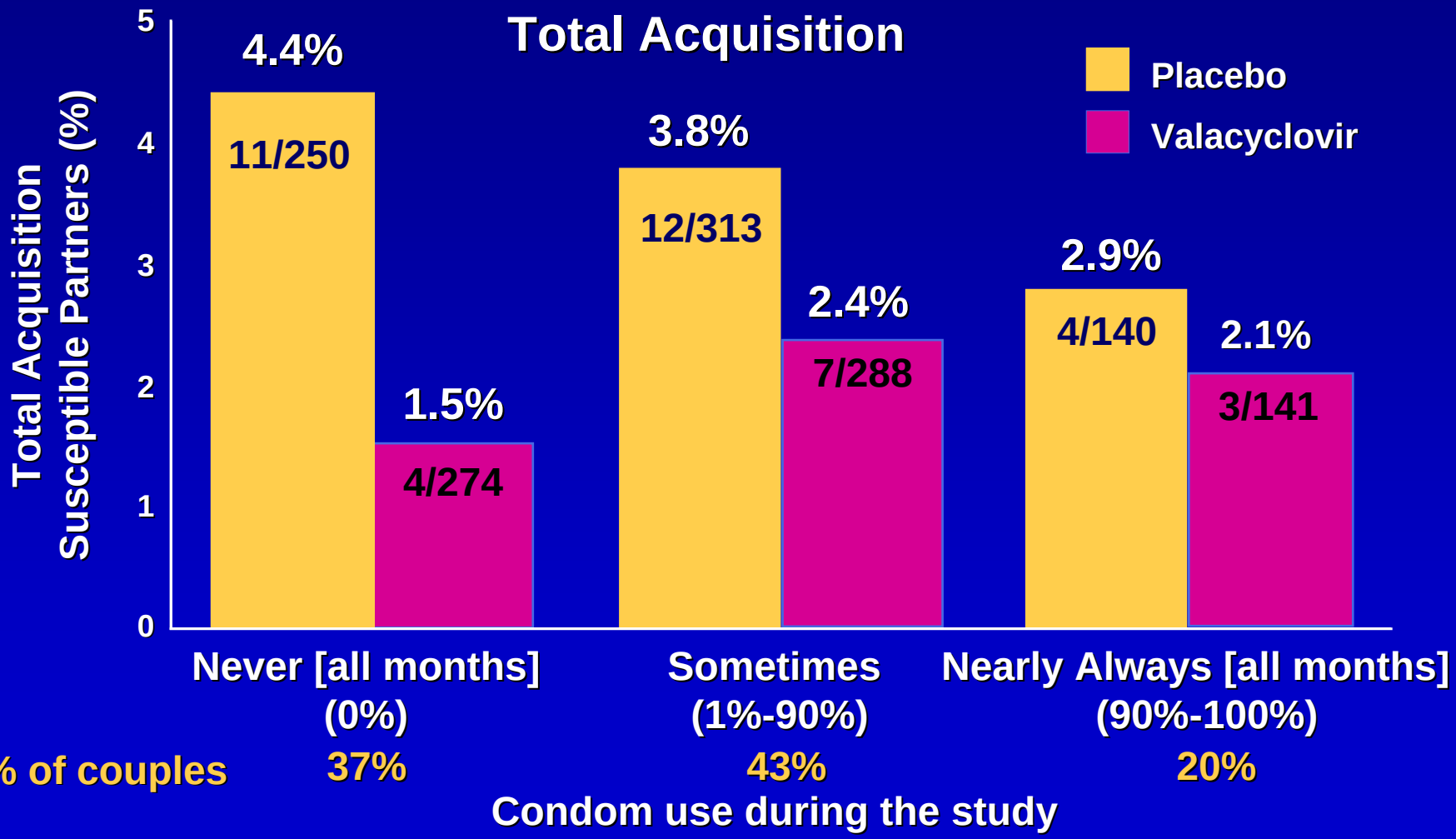
Rates of Transmission of HSV-2 to Susceptible Partners is Reduced with Once-Daily Suppressive Therapy

- 1484 heterosexual couples randomly assigned to take 500 mg of valacyclovir or placebo once daily for 8 months
- Serum samples collected monthly from susceptible partners for HSV analysis
- The valacyclovir group showed
  - decreased transmission
  - lower frequency of shedding
  - fewer copies of HSV-2 DNA when shedding occurred



Corey et al, NEJM 2004; 350:11-20

Valacyclovir and Condom Use to Prevent HSV Transmission



Corey L et al. N Engl J Med. 2004;350:11-20.

Valtrex® Direct Marketing

"VALTREX is the only medication proven to reduce the risk of spreading genital herpes to a partner. "

HSV Screening and Treatment Goals

- To reduce HSV transmission
  - Antiviral treatment at suppression dose
  - Indications may include: discordant couples, persons with multiple partners, HIV infected
  - Reassess discordant partner annually for seroconversion
  - Counsel regarding condoms, disclosure, abstinence
- To reduce HIV transmission
  - Genital HSV-2 (even asymptomatic) increases risk of transmitting and acquiring HIV
  - Suppressive therapy aimed at HSV-2 may also suppresses genital HIV
  - Cost-effectiveness depends on test, drug, prevalence of HSV-2 and HIV
    - Complex; may require setting-specific decisions

Genital HPV Infection in the U.S.

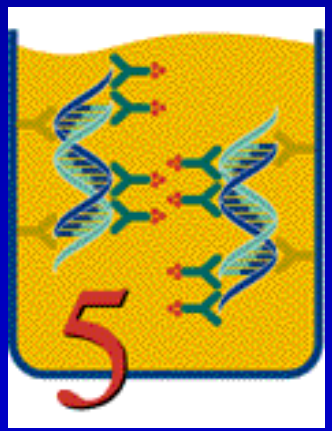
- 20 million people currently infected
- 6.2 million new infections annually
- Up to 80% of sexually active people acquire HPV at some point in their lives

W. Cates, STD 1999; Weinstock, Persp Sexual Repro Health 2004

HPV DNA Test

RNA probe cocktails to the most common cancer-associated HPV types:

16, 18,
31, 33, 35, 39, 45,
51, 52, 56, 58, 59, & 68



Digene Hybrid Capture II

Clinical Indications for HPV DNA Testing

FDA-cleared for:

- Triage of ASCUS
- Adjunct screening in women age 30 and over

Supported by research:

- 12-month f/u of LSIL in adolescents
- Follow-up management of:
  - No CIN on colpo
  - Biopsy-proven CIN I
  - Post treatment CIN II & III

NO ROLE **for HPV DNA Testing**

- Screening in women under 30
- Diagnosis of genital warts
- Testing in males
- Triage of ASC-H, LSIL or higher grade lesions
- Evaluation of sexually active female prior to vaccination
- Patients diagnosed with non-HPV STD
- Partners of patients with warts or non-HPV STD

STD Screening for Women

- Adolescents and women up to age 25
  - Annual chlamydia screening
  - Gonorrhea screening based on risk factors if low prevalence
  - Others STDs based on risk
  - HIV (?)
  - HSV (?)
- Women over 25 years of age
  - Based on risk factors
    - Multiple partners, partner may have other partner(s)

STD Screening Recommendations for Pregnant Women

- Pregnant women at first prenatal visit
  - HIV, Syphilis serology, HepBsAg
  - Chlamydia for all women or based on age and risk
  - Gonorrhea based on age and risk
  - Hep C based on risk
  - BV if previous high risk pregnancy
- Pregnant women early in the 3rd trimester and at delivery
  - If continued risk or new risk
  - If positive STD screen at first prenatal visit

STD Screening for MSM

- All MSM
  - HIV
  - Syphilis
  - Urethral CT and GC
  - HSV (?)
- Patients who report receptive anal sex
  - Rectal gonorrhea
  - Rectal chlamydia
- Patients who report receptive oral sex
  - Pharyngeal gonorrhea

- Annually for all MSM
- Every 3-6 months if high risk behavior
  - Multiple anonymous partners, meth use

Questions ???